

AUTHOR: Meyaard Linde; Hovenkamp Egbert; Pakker Nadine; Van Der Pouw Kraan
Tineke C T M; Miedema Frank(a)
AUTHOR ADDRESS: (a)Dep. Clin. Viro-Immunol., Central Lab. Netherlands Red
Cross Blood Transfusion Serv., Plesmanlaan, Netherlands

JOURNAL: Blood 89 (2):p570-576 1997
ISSN: 0006-4971
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: The role of interleukin-12 (**IL-12**) in Th1 cell differentiation is well established. The heterodimer p70, composed of a p40 and a p35 chain, is the biologically active form. **IL-12** production by human monocytes is enhanced by interferon-gamma (IFN-gamma) and inhibited by IL-10 and prostaglandin E-2 (PGE-2). Peripheral blood mononuclear cells from human immunodeficiency virus (HIV)-infected individuals reportedly have impaired **IL-12** p40 and p70 production on stimulation with Staphylococcus aureus Cowan I (SAC) in vitro. Both PGE-2 and IL-10 previously were proposed to be instrumental in this defect in **IL-12** production. Here, we studied **IL-12** p40 and p70 production in relation to IL-10 and PGE-2 production in whole blood cultures from HIV-infected individuals. On stimulation with lipopolysaccharide, **IL-12** production was normal. However, on stimulation with SAC, **IL-12** p40 and p70 production was decreased in HIV-infected individuals and correlated significantly with decreased peripheral blood CD4+ T-cell number and T-cell reactivity to CD3 **monoclonal antibody** in vitro. However, IL-10 and PGE-2 production in cultures from HIV-infected individuals was normal and did not relate to **IL-12** production. In conclusion, **IL-12** production by cells from HIV-infected individuals is impaired under certain conditions in vitro

3-10-99
Search

? s monoclonal(w)antibod?

408393 MONOCLONAL
1284882 ANTIBOD?
S3 336837 MONOCLONAL(W)ANTIBOD?
? s S3 and IL-12

336837 S3
234 IL-12
S4 6 S3 AND IL-12
? s S4 and IL(w)12

6 S4
195994 IL
1169949 12
7117 IL(W)12
S5 6 S4 AND IL(W)12
? T S5/7/all

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DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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11522333 BIOSIS NO.: 199800303665
Peritransplant tolerance induction with anti-CD3-immunotoxin: A matter of
proinflammatory cytokine control.

AUTHOR: Contreras Juan L; Wang Pei X; Eckhoff Devin E; Lobashevsky Andrew L
; Asiedu Clement; Frenette Luc; Robbin Michelle L; Hubbard William J;
Cartner Samuel; Nadler Steven; Cook William J; Sharff Joshua; Shiloach
Joseph; Thomas Francis T; Neville David M Jr; Thomas Judith M
AUTHOR ADDRESS: UAB Transplant Cent., Boshell Diabetes Build. 802, 1808
7th Street South, Birmingham, AL 35294-0012, USA

JOURNAL: Transplantation (Baltimore) 65 (9):p1159-1169 May 15, 1998
ISSN: 0041-1337
DOCUMENT TYPE: Article
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: Background. Tolerance is gaining momentum as an approach to
reduce lifelong immunosuppressive therapy while improving transplant
longevity. Anti-CD3 immunotoxin (IT), FN18-CRM9, has potential to induce
tolerance owing to its exceptional ability to deplete sessile lymph node
T cells. However, if initiated at the time of transplantation,
alpha-CD3-IT alone elicits a proinflammatory cytokine response,
precluding establishment of tolerance. Methods. Four groups of rhesus
monkeys received kidney allografts and immunosuppression. Three groups
received alpha-CD3-IT alone or alpha-CD3-IT supplemented with
15-deoxyspergualin (DSG) and/or methylprednisolone (MP). One group
received alpha-CD3-**monoclonal antibody** with DSG and MP.
Cytokines were measured by enzyme-linked immunosorbent assay. Results:
Supplementing peritransplant alpha-CD3-IT treatment with a brief course
of DSG and MP promoted rejection-kidney allograft acceptance in 75% of
macaques followed for up to 550 days. Among those given alpha-CD3-IT
alone or with MP, none were long-term survivors. Tolerance developed
after alphaCD3- IT, DSG, and MP treatment, but not when the unconjugated
alpha-CD3 **monoclonal antibody** was substituted for IT.

Systemic production of proinflammatory cytokines interferon-gamma (IFN-gamma) and tumor necrosis factor-alpha induced after peritransplant alpha-CD3-IT was prevented only in animals given DSG. Despite high levels of interleukin (IL)-12 in the first month after transplant, tolerant recipients exhibited IL-12 resistance, as evidenced by baseline plasma levels of IFN-gamma but elevated HA. DSG was shown to inhibit IL-12-driven IFN-gamma production by a mechanism associated with inhibition of nuclear factor kappa-B. Conclusions. In this model, peritransplant induction of tolerance is promoted by efficient elimination of sessile lymph node T cells and control of the proinflammatory IFN-gamma response by a mechanism that appears to involve resistance to IL-12.

5/7/2 (Item 2 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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11217412 BIOSIS NO.: 199799838557
Active specific immunotherapy with mouse anti-idiotypic (anti-id) mAb MK2-23.

AUTHOR: Ferrone S; Desai S; Wang X; Zhang D; Noronha E; Kymisses A
AUTHOR ADDRESS: New York Med. Coll., Dep. Microbiol. Immunol., Basic Sci. Build., Room 308, Valhalla, NY 10595, USA

JOURNAL: International Journal of Oncology 11 (SUPPL.):p932 1997

CONFERENCE/MEETING: 2nd World Congress on Advances in Oncology Athens, Greece October 16-18, 1997
ISSN: 1019-6439
RECORD TYPE: Citation
LANGUAGE: English

5/7/3 (Item 3 from file: 55)
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11165990 BIOSIS NO.: 199799787135
Autoantibody production and cytokine profiles of MHC class I (beta-2-microglobulin) gene deleted New Zealand Black (NZB) mice.

AUTHOR: Chen Shao-Yuan; Takeoka Yuichi; Pike-Nobile Larry; Ansari Aftab A; Boyd Richard; Gershwin M Eric(a)
AUTHOR ADDRESS: (a)Div. Rheumatol., Allergy and Clin. Immunol., Sch. Med., Univ. Calif. at Davis, Davis, CA 95616, USA

JOURNAL: Clinical Immunology and Immunopathology 84 (3):p318-327 1997
ISSN: 0090-1229
RECORD TYPE: Abstract
LANGUAGE: English

ABSTRACT: We established a colony of MHC class I deleted (knockout) NZB mice, which lack the beta-2 microglobulin gene (NZB.beta-2m-/-), to characterize the contribution of MHC class I to the thymic microenvironment abnormalities, autoantibody production and lupus-like disease of NZB mice. Using an extensive panel of well characterized **monoclonal antibodies** defining thymic epithelial and other stromal elements, we demonstrated that deletion of MHC class I molecules does not change the thymic abnormalities, including the presence of a cortical epithelial cell free region, ectopic expression of medullary epithelial antigens, and the irregular shape of the medullary epithelial network of NZB mice. Moreover, the decreased staining of MTS 33+ cells, a marker of premature thymocyte maturation, was also seen in

NZB.beta-2m-/- . However, although NZB cntdot beta-2m-/- mice had approximately the same levels of IgM and IgG anti-ss and dsDNA antibodies when compared to control NZB mice, there were significant alterations in the incidence and onset of anti-erythrocyte antibody levels. NZB.beta-2m-/- had a lower incidence and a delayed onset of anti-erythrocyte autoantibody production compared to that seen in NZB mice. We also compared constitutive and PHA-P-driven levels of IFN-gamma, IL-4, IL-6, and **IL-12** in cells from NZB, NZB.beta-2-/-, and control C57BL/6 mice. Mitogen stimulated cells showed a decreased IFN-gamma, and a marked increase in IL-6 and **IL-12** in NZB and NZB.beta-2m-/- mice.

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11047884 BIOSIS NO.: 199799669029
Modulation of the expression of membrane-bound regulators of complement activation on renal tumor cell lines by cytokines.

AUTHOR: Gorter A(a); Blok V T(a); Tijsma O(a); Daha M R; Fleuren G J(a)
AUTHOR ADDRESS: (a)Dep. Pathol., Leiden Univ. Hosp., Leiden, Netherlands

JOURNAL: Experimental and Clinical Immunogenetics 14 (1):p92 1997

CONFERENCE/MEETING: 6th European Meeting on Complement in Human Disease
Innsbruck, Austria March 12-15, 1997
ISSN: 0254-9670
RECORD TYPE: Citation
LANGUAGE: English

5/7/5 (Item 5 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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10823461 BIOSIS NO.: 199799444606
Regulation of **IL-12** enhanced NK cytotoxicity by
monoclonal antibody against ICAM-1 molecules in NK cells.

AUTHOR: Cho D H(a); Song H K(a); Kang H S(a); Yoon S R(a); Lee H G(a); Pyun
K H(a); Lee W J; Rothlein R; Kim Y B; Choi I(a)
AUTHOR ADDRESS: (a)KRIBB, Taejon, South Korea

JOURNAL: Journal of Allergy and Clinical Immunology 99 (1 PART 2):pS465
1997

CONFERENCE/MEETING: Joint Meeting of the American Academy of Allergy,
Asthma and Immunology, the American Association of Immunologists and the
Clinical Immunology Society San Francisco, California, USA February
21-26, 1997
ISSN: 0091-6749
RECORD TYPE: Citation
LANGUAGE: English

5/7/6 (Item 6 from file: 55)
DIALOG(R)File 55:BIOSIS PREVIEWS(R)
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10759886 BIOSIS NO.: 199799381031
Interleukin-12 (**IL-12**) production in whole blood cultures from
human immunodeficiency virus-infected individuals studies in relation to
IL-10 and prostaglandin E-2 production.

6. DIALOG(R) Document Delivery
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Custer, Tara

From: Custer, Tara
Sent: Friday, February 12, 1999 2:52 PM
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Subject: Case ~~09/174,656~~ *09/232,522*

Please send the following articles to my mailbox ASAP:

1. Clin. Immunol. and Immunopathol. 84 (3): p 318-327 1997
2. J. of Allergy and Clin. Immunology 99; (1 part 2); pS465
3. Blood 89: (2): p570-576 1997

Thanks

Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
CM1 9D04
Mail Room 9OC1

Custer, Tara

From:

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Monday, March 1, 1999

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TEXT SEARCH

Please search the attached claims (1-33 only), along with search of inventors (on biblio sheet) and return results along with copy of claims to my mailbox. A copy of the claims is enclosed. Thanks.

The invention and some key words/search terms are listed:

1. A monoclonal humanized antibody to the human IL-12 p75 heterodimer which consists of a p35 subunit and a p40 subunit forming a p75 heterodimer wherein the monoclonal antibody
 - a. Reacts w/an epitope presented by the p75 heterodimer of human IL-12 but is not reactive with any epitope presented by said p40 subunit
 - b. Is produced from a cell line of the mouse which is deficient in the gene encoding said p35 subunit or the p40 subunit of IL-12
 - c. Cross reacts w/ the rhesus monkey IL-12
 - d. Produced by a hybridoma having ATCC # HB-12446, 12447, 12448, or 12449
 - e. Neutralizes 90% of the bioactivity of human IL-12 by inhibiting IL-12 stimulated PHA-activated human lymphoblast proliferation (IFN-gamma production) wherein the concentration of the antibody is 0.5 ug/mL and the concentration of human IL-12 is 0.25 ng/mL
 2. A hybridoma capable of producing the monoclonal antibody mentioned above
- S (IL-12 or cytotoxic(w)lymphocyte(w)maturation(w)factor or NK(w)CSF or natural(w)killer(w)cell(w)stimulatory(w)factor or heterodimeric(w)cytokine? Or NK(w)LAK or
- S L1 and (p35? And p40?) or (35 kDa and 40kDa) and (p75? Or 75kDa) *epitope? or subunit?*
- S L2 and (monoclonal(w)antibod? Or antagonist? Or heterodimeric(w)specific(w)antibod? Or 16F2 or 16G2 or 20E11 or 5F2 or 20C2) *→ or 5F2, 16F2, 16G2, 20E11, 20C2,*
- S L2 and (humaniz?) *→ or SP2/0 or NS/O*
- S L3 and cell(w)line? And (mouse? Or mammal? Or knock(w)out)
- S L4 and (monkey? ~~or rhesus?~~ *or rhesus?*)
- S L5 and (hybridoma? Or HB12447) *or ATCC?*
- S L6 and (neutraliz? Or deplet? Or destroy? Or decreas? Or downregulat?) *or inhibit or block*
- S L7 and (PHA? Or phytohemagglutinin?) *humanized lymphoblasts or lymphoblasts?*
- S L8 and IFN?
- S L9 and (lymphoblast?(w)proliferation?)
- S L10 and (concentration? Or .25(w)ng(w)mL or .5(w)ug(w)mL)
- S L11 and (deficient? Or lack? Or mutat?(p)(p35? And p40?)
- S L12 and (immunoassay? Or ELISA? Or lymphocyte(w)proliferation(w)assay?) *competitive(w), immunoassay (w)assay cross (block) binding assay?*
- I have R6P (w) monkey or rhesus and cross react*

All relevant references can be printed

Thanks.

Tara L. Custer

Patent Examiner

Art Unit 1644

(703) 305-1690

Building CM1 Room 9D04

*Neutralize in vivo
rhesus monkey
activity*

Custer, Tara

From: Custer, Tara
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1. Clin. Immunol. and Immunopathol. 84 (3): p 318-327 1997
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3. Blood 89: (2): p570-576 1997

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Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
CM1 9D04
Mail Room 9OC1

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1. Hybridoma; 1997 Aug.; 16(4); 363-9
2. J. of Immunol.; March 1998; 160(5); 2174-9
3. Ann. Review of Immunol.; 1998; 16; 495-521
4. Infection and Immunity; Nov. 1997; 65(11); 4734-7
5. Eur. Journal of Immunol.; 1997; Jan.; 27 (1); 147-54
6. J. Allergy and Clinical immunology; 1997; Vol. 99; No. 1; part 2; p. S52
7. Proc. Natl. Acad Sci.; 1996; Nov. 26; 93(24); 14002-7
8. FASEB Journal; 1996; Vol. 10; No. 6; p. A1323
9. FASEB Journal; 1996; Vol. 10; No. 6; p. A1310
10. Annals of the NY Acad. of Sci. ; 1996; Oct 31; 795; 390-3
11. Eur. J. Immunol.; Feb. 1996; 26(2); 345-50
12. J. of Immunological Methods; Jan. 1996; 189(1); 15-24
13. Annals of NY Acad of Sciences; 1996 Oct. 795; 1-12
14. J. Biol. Chem.; 1995; (17); 270 (11); 5864-71
15. Research in Immunology; 1995 Sep-Oct.; 146; (7-8); 439-45
16. 9th International Congress of Immunol.; 1995; pp. 299; July 23-29
17. Eur. J. of Immunology; 1995; 25 (1); 200-6
18. FASEB Journal; 1994; Vol. 8; No. 4-5; p. A963;
19. J. Immunology; 1994; 153 (1); 128-36



Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
CM1 9D04
Mail Room 9OC1

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1. *Proc. Natl. Acad. Sci.*; Vol. 88; 4143
2. *J. Immunol.*; 1991; 146; 3074
3. *Arch. Biochem. Biophys.* 294:230; 1992
4. *J. Exp. Med.*; 176: 1387; 1992
5. *J. Immunol.*; 154; 116; 1995
6. *Eur. J. Immunol.*; 25:200; 1995
7. *Cytokine*; 6; 8A2a; 1994
8. *Eur. J. Immunol.*; 26:1553-59; 1996
9. *Immunity*; 4:471-481 (1996)

Tara L. Custer
Patent Examiner
Art Unit 1644
(703) 305-1690
CM1 9D04
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1. J. Immunol.; 147; 1548 (1991)

Tara L. Custer
Patent Examiner
Art Unit 1644
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1. J. Immunol.; 153; 128 (1994)

Tara L. Custer
Patent Examiner
Art Unit 1644
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